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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/679,913	10/06/2003	James Ronald Lawter	ORA5005USANP(J&JO-105US)	2961

23579 7590 01/18/2007

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EXAMINER	
JAGOE, DONNA A	
ART UNIT	**PAPER NUMBER**
1614	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/18/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/679,913	LAWTER, JAMES RONALD	
	Examiner	Art Unit	
	Donna Jagoe	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-18 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-18 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 3/9/04.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-18 are presented for examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 18 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment of oral mucositis resulting from radiation or chemotherapy, it does not reasonably provide enablement for prevention of oral mucositis. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, predictability of the prior art, state of the prior art and the amount of experimentation necessary. All of the **Wands factors** have been considered with regard to the instant claims, with the most relevant factors discussed below.

A. Breath of the Claims: The complex of nature of the claim is greatly exacerbated by breath of the claim. The claims encompass oral mucositis resulting from radiation or chemotherapy (Chemotherapy and radiation therapy

can affect the ability of cells to reproduce, slowing healing of the oral mucosa. Radiation therapy to the head and neck area frequently results in a loss of taste perception, decreased production of saliva, along with inflammation of the mouth lining (mucositis), pain and difficulty swallowing.). Each of these defects may or may not be addressed by the administration of the claimed compounds.

B. Nature of the Invention: Claim 18 is drawn to a method of treating or preventing oral mucositis resulting from radiation or chemotherapy for cancer comprising administering an effective amount of a composition comprising a tetracycline and a pharmaceutically acceptable mucoadhesive polymer, a viscous polymer gel or a hydrogel. The nature of the invention is extremely complex in that it encompasses the actual prevention of oral mucositis resulting from radiation or chemotherapy such that the subject treated with above compounds does not contract oral mucositis.

C. State of the Prior Art: While the state of the art is relatively high with regard to **treatment** or oral mucositis, the state of the art with regard to **prevention** of such disorders is underdeveloped. In particular, there do not appear to be any examples or teachings in the prior art wherein a compound similar to the claimed compounds was effective in **preventing** development of oral mucositis from cancer and radiation therapy.

D. The Level of One of Ordinary Skill: The relative skill of those in the art is generally that of an MD or DO.

E. Predictability of the Art: The lack of significant guidance from the specification or prior art with regard to the actual **prevention** of oral mucositis from cancer and radiation therapy with the claimed compounds makes practicing the claimed invention unpredictable in terms of prevention of oral mucositis from cancer and radiation therapy.

F. Guidance of the Specification: The guidance given by the specification as to how one would administered the claimed compounds to a subject in order to actually prevent oral mucositis from cancer and radiation therapy is minimal. All of the guidance provided by the specification is directed towards **treatment** rather than prevention of oral mucositis from cancer and radiation therapy.

G. Working Examples: All of the working examples provided by the specification are directed toward the treatment rather than prevention of oral mucositis from cancer and radiation therapy.

H. The amount of Experimentation Necessary: In order to practice claimed invention, one of skilled in the art would have to first envision a combination of appropriate pharmaceutical carrier, compound dosage, duration of treatment, route of administration, etc. and appropriate animal model system for one of the claimed compounds and test the combination in the model system to determine whether or not the combination is effective for **prevention** of oral mucositis from cancer and radiation therapy. If unsuccessful, which is likely, given the lack of significant guidance from the specification or prior art with regard to prevention of oral mucositis from cancer and radiation therapy with any compound, one of skill

in the art would have to then either envision a modification of the pharmaceutical composition of claim 1, composition dosage, duration of treatment, route of administration, etc. and appropriate animal model system, or envision an entirely new combination of the above, and test the system again. If again unsuccessful, which is likely given the lack of significant guidance from the specification of prior art regarding prevention of oral mucositis from cancer and radiation therapy with any compound, the entire, unpredictable process would have to be repeated until successful. Therefore, it would require undue, unpredictable experimentation to practice the claimed invention to prevent the development of oral mucositis from cancer and radiation therapy in a subject by administration of the composition of claim 18.

Therefore, a method of **preventing** in a subject oral mucositis from cancer and radiation therapy by administering the pharmaceutical composition of claim 18 is not considered to be enabled by the instant specification.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5, 7-9, 12 and 17-18 are rejected under 35 U.S.C. 102(b) as being anticipated by Orapharma Inc. WO 01/19362 A2.

Orapharma Inc. teaches a composition for treatment of the oral mucosa comprising tetracycline (page 5, line 17 to page 6, line 25) and a mucoadhesive polymer (page 7, line 15 to page 9, line 15), including natural polymers such as carageenan and pectin (page 9, lines 8-9). The tetracycline is poorly absorbed, in a pharmaceutically acceptable salt or base (see abstract). Meclocycline is contemplated in the invention of Orapharma Inc (see examples 1-14) to treat or prevent oral mucositis. Regarding the cationic polymer of claim 2, for clarification of what is meant by a cationic polymer, the instant specification was consulted. Page 3 of the instant specification defines a cationic polymer as "any pharmaceutically acceptable natural or synthetic polymer, which has the desired physical or chemical properties to enhance retention in the mouth. Polymers will typically be cationic polymers, mucoadhesive polymers or polymers, which form a gel or hydrogel that physically, adheres to the mucosa. Since the polymers of Orapharma Inc. fits this definition it is clearly anticipated by Orapharma. Rapid release hydrogel carriers of tetracycline are provided in Orapharma Inc. Page 10 wherein the solids designed to be dissolved to prepare a liquid dosage form prior to administration are rapidly dissolving and include particle size reduction and optimization of the H of the dissolution medium. Compositions that dissolve in the mouth and semisolids are disclosed in Orapharma inc. (sustained or controlled release tetracycline of instant claim 12) (page 7, line 30-33). Methods are provided to treat or prevent oral mucositis from radiation or chemotherapy for cancer (see page 1) comprising an effective amount of a tetracycline and a mucoadhesive polymer carrier (page 7, line 15 to page 9, line 15).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 6, 10, 11 and 13-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Orapharma Inc. WO 01/19362 A2.

Claim 6 is drawn to an amorphous tetracycline, claim 10 is drawn to the mucoadhesive polymer that ionizes to form a cationic polymer upon contact with an aqueous medium, claim 11 is drawn to the composition wherein the polymer is a polyamine, claims 12, 13 and 16 are drawn to polymers selected from chitosan, gelatin and fish gelatin. Claim 15 is drawn to the gelatin with an isoelectric point of 7 or more. Orapharma Inc. teaches composition for treatment of the oral mucosa comprising tetracycline (page 5, line 17 to page 6, line 25) and a mucoadhesive polymer (page 7, line 15 to page 9, line 15), including natural polymers such as carageenan and pectin

(page 9, lines 8-9). Although it doesn't specifically recite the amorphous tetracycline, it would have been obvious to vary the type of tetracycline employed motivated by the desire for a slow release type tetracycline for treatment of mucositis. The natural polymers chitosan and gelatin and fish gelatin are not specifically recited. However, It is prima facie obvious to substitute equivalents, motivated by the reasonable expectation that the respective species will behave in a comparable manner or give comparable results in comparable circumstances. *In re Ruff* 118 USPQ 343; *In re Jezel* 158 USPQ 99; the express suggestion to substitute one equivalent for another need not be present to render the substitution obvious. *In re Font*, 213 USPQ 532. It would have been made obvious to one of ordinary skill in art at the time it was made to substitute the natural polymers gelatin and chitosan for the natural polymers carageenan and pectin motivated by the need for a polymer carrier that is safe and effective in forming a film on the mucosal surfaces. Regarding the gelatin with an isoelectric point of 7 or more, as noted in *In re Best* (195 USPQ 430 (CCPA 1977)), and *In re Fitzgerald* (205 USPQ 594 (CCPA 1980)), the mere recitation of newly-discovered function or property, inherently possessed by things in prior art, does not cause claims drawn to those things to distinguish over prior art. In such a situation, the burden is shifted to the applicant to prove that subject matter shown to be in prior art does not possess characteristic relied on where it has reason to believe that functional limitation asserted to be critical for establishing novelty in claimed subject matter may be inherent characteristic of prior art.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-18 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-24 of copending Application No. 11/230397. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant and conflicting claims recite substantially the same subject matter, differing only in the description of the particular components claimed. For instance, conflicting claims 1-8 recite the structure of the tetracycline compositions that are encompassed by the broad claim "a tetracycline" in the instant claims. Further, the methods of conflicting claims 15-24 recite substantially the same subject matter, the method of treating or preventing oral mucositis resulting from radiation or chemotherapy for cancer comprising administering a tetracycline in a topical

carrier. It would have been obvious to anyone of ordinary skill in the art that the claims overlapped in scope in this manner. One skilled in the art would have been motivated to have interpreted the claims as broadly as is reasonable, and in doing so recognize that they are coextensive in scope and thus the proper subject of an obviousness-type double patenting rejection as outlined by *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970). This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim 18 is rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-11 of U.S. Patent No. 6,683,067. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant and conflicting claims recite substantially the same subject matter, differing only in the description of the particular components claimed. For instance, conflicting claim 1 requires a method of treating mucositis comprising administering a poorly absorbed tetracycline in a carrier for topical. Instant claim 18 is broadly inclusive thereof in that it recites tetracycline for oral mucositis from radiation or chemotherapy of cancer. It would have been obvious to anyone of ordinary skill in the art that the claims overlapped in scope in this manner. One skilled in the art would have been motivated to have interpreted the claims as broadly as is reasonable, and in doing so recognize that they are coextensive in scope and thus the proper subject of an obviousness-type double patenting rejection as outlined by *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

Claims 1-17 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-11 of U.S. Patent No. 6,893,665. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant and conflicting claims recite substantially the same subject matter, differing only in the description of the particular components claimed. For instance, conflicting claim 1 requires a composition comprising a tetracycline in the form of a polyvalent metal ion complex. Instant claim 1 is broadly inclusive thereof in that it recites a tetracycline. The instant claims differ from the reference in claiming a broader scope. It would have been obvious to anyone of ordinary skill in the art that the claims overlapped in scope in this manner. One skilled in the art would have been motivated to have interpreted the claims as broadly as is reasonable, and in doing so recognize that they are coextensive in scope and thus the proper subject of an obviousness-type double patenting rejection as outlined by *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

Claims 1-17 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-14 of U.S. Patent No. 6,946,118. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant and conflicting claims recite substantially the same subject matter, differing only in the description of the particular components claimed. For instance, conflicting claim 1 requires a composition comprising a poorly absorbed tetracycline. Instant claim 1 is broadly inclusive thereof in that it recites a tetracycline. The instant claims differ from the reference in claiming a broader scope. It would have

been obvious to anyone of ordinary skill in the art that the claims overlapped in scope in this manner. One skilled in the art would have been motivated to have interpreted the claims as broadly as is reasonable, and in doing so recognize that they are coextensive in scope and thus the proper subject of an obviousness-type double patenting rejection as outlined by *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

Thus the claims fail to patentably distinguish over the state of the art as represented by the cited references.

Accordingly, for the above reasons, the claims are deemed properly rejected and none are allowed.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Donna Jagoe whose telephone number is (571) 272-0576. The examiner can normally be reached on Monday through Thursday from 9:00 A.M. - 3:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Donna Jagoe
Patent Examiner
Art Unit 1614

January 5, 2007

ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER